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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/732,520	12/07/2000	John Roderick Morrison	14390	1130

7590 05/12/2003

Attn: Leopold Presser, Esq.
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EXAMINER	
FALK, ANNE MARIE	

ART UNIT	PAPER NUMBER
1632	16

DATE MAILED: 05/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

File

Office Action Summary	Application No.	Applicant(s)	
	09/732,520	MORRISON ET AL.	
	Examiner	Art Unit	
	Anne-Marie Falk, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the c ver sheet with the correspondence address --

P ri d f r Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 February 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disp sition of Claims

4)☒ Claim(s) *1-21 and 33-66* is/are pending in the application.

4a) Of the above claim(s) *1-21 and 33-44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *45-66* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The amendment filed February 19, 2003 (Paper No. 15) has been entered. Claims 22-32 have been cancelled. Claims 45-66 have been newly added.

Accordingly, Claims 1-21 and 33-66 are pending in the instant application.

Claims 1-21 and 33-44 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention. Applicant timely traversed the restriction requirement in Paper No. 12.

Claims 45-66 are examined herein.

The following rejections are reiterated or newly applied and constitute the complete set of rejections being applied to the instant application. Rejections and objections not reiterated from the previous office action are hereby withdrawn.

Specification

The amendment filed February 19, 2003 (Paper No. 15) is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: the amendment to the specification at pages 30 and 31, which indicates that **rats** were used in the experiments of Example 12. Applicants have not submitted any evidence to verify that rats were used in the experiments.

Applicant is required to cancel the new matter in the reply to this Office Action.

Alternatively, Applicants could file a declaration confirming that rats were used in the experiments of Example 12.

The disclosure is objected to because of the following informalities:

In Example 12, on page 30, at line 18 and page 31, at line 14, the specification refers to "animals" but does not indicate what animal species was used in the example. Since nuclear transfer techniques vary depending on the animal species used, identification of the animal species used in the example is an essential teaching for those of skill in the art.

In the table on page 32, the first column heading reads "transfected embryonic fibroblast," but there is no guidance regarding what was used to transfect the fibroblast.

Appropriate correction is required.

At page 6, paragraph 1 of the response, Applicants point to the specification at pages 16 to 17 for providing guidance regarding the use of a construct comprising a lacZ gene to transfect the fibroblasts. However, there is nothing in the specification to suggest that the transfected fibroblasts used in Example 13 carried the lacZ gene. Thus, it remains unclear what was used to transfect the fibroblast.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 45-66 are rejected under 35 U.S.C. 112, first paragraph, for reasons of record advanced on pages 4-7 of the Office Action of Paper No. 13 (mailed 8/9/02) as applied to Claims 22-32, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are directed to (i) a method of producing a non-human embryo by nuclear transfer, using a neural stem cell as the source of the donor nucleus, (ii) a method of producing a genetically

modified non-human animal by nuclear transfer, and (iii) a method of producing a cell line from an embryo to produce cloned cells of an embryo.

At page 7, paragraph 3 of the response, Applicants argue that the protocols used to isolate and propagate neural stem cells (NSC) are essentially the same in all mammalian species from which neural stem cells have thus far been isolated. However, the ability to isolate and propagate neural stem cells is not at issue here. The issues brought up in the initial rejection relate specifically to cloning procedures, not to the isolation and propagation of neural stem cells. Applicants jump to the conclusion that "the technology is applicable to all animals" ostensibly because "the protocols used to isolate and propagate NSC are essentially the same in all mammalian species from which neural stem cells have thus far been isolated." Although it is unclear to what "technology" Applicants are referring, there is no basis for jumping to the conclusion that methods of **cloning** by nuclear transfer are applicable to all animals just because protocols exist for isolating and propagating NSCs from a variety of species. The parameters affecting the success of nuclear transfer were discussed in the previous Office Action. Westhusin et al. (2001) report that "[w]ithout a doubt, one of the major factors influencing the probability of cloning a specific animal is species" (page 36, paragraph 3). As of the filing date of this application, December 2000, the art contained no reports of cloned rats. See Westhusin et al. (2001), particularly the abstract and page 39, paragraph 4.

At page 7, paragraph 4 of the response, Applicants assert that neural stem cells show similar characteristics across species, including potential to differentiate into all neural tissue, propensity to grow in spheres in culture, and ability to transdifferentiate into different tissue types. However, as discussed above, the properties of neural stem cells across species is not at issue here. The issues brought up in the initial rejection relate specifically to cloning procedures, not to the characteristics of neural stem cells.

At page 7, paragraph 5 of the response, Applicants assert that the basic techniques for nuclear transfer are the same across all mammalian species and require the same technical skill and equipment.

No support is offered for this assertion. The art cited in the prior Office Action clearly teaches that there are differences among species that affect the success of nuclear transfer protocols and that difficulties have been encountered in trying to clone a number of species.

At page 8, paragraph 2 of the response, Applicants assert that although differences exist between species in the ability and efficiency with which embryos can be cultured *in vitro*, this can be overcome by transferring the reconstructed embryos directly to recipient animals as opposed to culturing them for a period *in vitro* before transfer. No support is offered for this assertion and there is no evidence to refute the teachings of the art cited in the previous Office Action, to suggest that the difficulties encountered in cloning various species could be overcome by routine experimentation or by simply transferring reconstructed embryos immediately without first culturing them.

At page 8, paragraph 3 of the response, Applicants contend that the disclosure describes that the use of neural stem cells in nuclear transfer procedures in the rat can readily be replicated in other species by those of skill in the art, with little or no variance from the basic methodologies described. Applicants further contend that the basis for using neural stem cells as the nuclear donor, i.e., that NSCs are a cell type with the potential to develop into a range of tissues, is valid across all mammals, not just rats. Applicants conclude that the description and enablement of the technology in one mammalian species by the present invention, serves as validation of the approach in all mammalian species. No support is offered for the assertion that procedures used in the rat can readily be used in other species. Furthermore, with regard to the rat, the specification does not offer sufficient specific guidance to enable the method of producing a rat embryo or a rat. As pointed out previously, the art contained no reports of cloned rats as of the filing date of this application in December 2000.

At page 9, paragraph 2 of the response, Applicants point out that Example 13 of the specification shows that 78 rat embryos having NSC nuclei were obtained and transferred to recipient rats. However, no live born cloned rats resulted and there is no teaching that the embryos developed even to the

blastocyst stage. Moreover, the instant specification does not teach how to use such an early embryo for anything other than for producing a cloned animal. Thus, the specification does not provide sufficient guidance for making and using an embryo, including a rat embryo. Claims 45-62 are directed to producing an embryo. Although the claims encompass making a single-cell embryo, the specification does not teach how to use a single-cell embryo for anything other than making a cloned animal. Claims 65 and 66 include a step of culturing the embryo to an advanced cleavage stage embryo. However, the specification does not provide sufficient specific guidance for culturing an embryo or even a rat embryo produced by the method of the invention to an advanced cleavage stage embryo. Given the unpredictability in the art, for reasons of record, undue experimentation would have been required to practice the claimed methods.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 57, 62, 65, and 66 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 57 is indefinite in its recitation of "2 to 20 μ/ml" because a μ is a unit of measurement for length rather than mass.

Claim 62 is indefinite in its recitation of "destroying" and "deleting" because it is unclear how "destroying" would be distinguished from "deleting."

Applicants suggest that a "destroyed" gene is one that is disrupted or inactivated. However, the specification does not define "destroying" in these terms and one of skill in the art could just as easily understand it to be equivalent to "deleting." Clarifying claim language is needed. The Examiner agrees

that a "deleted" gene is one that has been removed, but this does not distinguish "deleting" from "destroying."

Claims 65 and 66 are indefinite in their recitation of "producing a cell line from an embryo to produced cloned cells of an embryo" in the preamble because there is no cloning step in the claims. Thus, the body of the claim is in conflict with the preamble.

Conclusion

No claims are allowed.

This application contains Claims 1-21 and 33-44 drawn to an invention nonelected with traverse in Paper No. 12. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne-Marie Falk whose telephone number is (703) 306-9155. The examiner can normally be reached Monday through Thursday and alternate Fridays from 10:00 AM to 7:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the patent analyst, William Phillips, whose telephone number is (703) 305-3482.

Anne-Marie Falk, Ph.D.

Anne-Marie Falk
ANNE-MARIE FALK, PH.D
PRIMARY EXAMINER